

## Foxboro pH sensor improves pharmaceutical product, process, profits

As a custom manufacturer of pharmaceutical ingredients, Raylo is faced with developing and scaling a wide range of chemistries and products, and ultimately delivering these on a commercial basis. “The compounds we produce are used in various human applications from cancer treatments to anti-virals,” says Rob Pastushak, senior technical supervisor of pharmaceutical manufacturing for Raylo. “Processes have to be controlled tightly in order to ensure quality and consistent high yields. While our products are generally high value, it is a competitive industry so delivering high yield to the customer is a must.”

“Batches typically range from 300 to 900 kilograms and even the slightest variation in our process has a significant impact on costs. If our process is off even slightly, the cost implications are significant. Over time, this could add up to substantial losses in production and profitability,” says Pastushak.



Another critical and ongoing challenge facing Raylo is demonstrating to its clients and the U.S. Food and Drug Administration (FDA), that the company has complete control over its production process. As a member of the Degussa Fine Chemicals Division, the Raylo, Edmonton, Alberta, Canada, facility is Current Good Manufacturing Practices (CGMP) certified. This quality standard assures that quality and repeatability are built into their production process. All of the company’s production equipment must be tested and certified, which involves a strict qualification process for regulatory compliance and regular

audits by the FDA. Raylo must document its process and ability to consistently deliver quality ingredients in the high volumes required.

“The majority of our business involves exports to the United States. If we don’t receive FDA approval, we will go out of business,” says Pastushak. “We must clearly demonstrate that we control every aspect of our manufacturing process at all times, and that our instruments are properly calibrated on a regular basis.”

### Problems with pH measurement

To assure consistent product quality and maximize batch yields, Raylo launched an effort in 2003 to improve the efficiency of its manufacturing process. Pastushak focused on pH measurement.

“Measuring pH was a problem at that time because of the unreliability of our pH sensors. They simply could not hold up under the aggressive chemicals that we use, such as hydrobromic acid. The organic solvent constituent caused the probe’s O-rings to degrade during the most critical

point of the process. In many cases, three probes, at approximately \$600 per probe, would fail during processing just one batch,” Pastushak says.

Once the O-ring degraded, the pH probes no longer provided accurate readings, which presented another problem for Raylo. The process calls for two phases of crystallization, each of which requires pH measurement with tight tolerances of plus or minus 0.1 of the target value. “Crystallization is critical and pH is king. When the chemical composition of a drug falls outside of the correct pH range, quality and yield suffer because maximum crystallization fails to occur,” says Pastushak.



Pastushak points out that given the competitive nature of the custom manufacturing business and the tight margins that exist in the industry, even a small variance in yield can have a huge impact on the bottom line. “A 1 or 2 percent increase in the target commercial yield is translated as 100 percent profit. Likewise, a consistent loss of 1 or 2 percent of the commercial target yield translates as lost profit. You don’t stay in business long with this type of performance,” says Pastushak.

### **Solving the pH puzzle**

To resolve the pH measurement issue, Pastushak researched several probes and decided to test the Foxboro 871PH Series sensor, from the Measurements & Instruments Division of Invensys Process Systems. The 871 is a rebuildable pH probe that incorporates patented technology from the award-winning Foxboro DolpHin™ pH sensor line.

“We found many vendors that offered quality sensors, but Foxboro was the only one that could provide a robust design that could stand up to all the reagents and solvents in our solutions. The 871’s Ryton® polymer plastic construction is compatible with all the materials in our process and is just what the doctor ordered for our demanding application,” says Pastushak.

### **Proven in process**

To ensure the sensor met quality standards, Raylo put the Foxboro 871PH through extensive testing before integrating the unit into the manufacturing process. During an initial one-month test, Raylo discovered that the 871PH allowed them to control pH faster by adjusting to solution changes during a shorter period of time. “The results have been consistent from batch to batch,” says Pastushak. “As soon as we add a solution to adjust pH, the probe responds immediately and provides the new pH reading. We’ve found it to be accurate to  $\pm 0.03$  pH units, which are well within our target limits.”

The fast response time and improved accuracy contribute to higher batch yields and ultimately profitability for Raylo. “We can now complete a pH adjustment in three hours rather than the 18 to 24 hours it previously took,” says Pastushak. “And we no longer have to take 40 samples to the lab to confirm measurement accuracy -- we only take one, as a matter of quality assurance protocol. Previously, every time we grabbed a lab sample, we had to put the process on hold

until we got the results back. This is significant when you consider not only the yield impact but the cost of a process hour,” says Pastushak.

This reduction in the number of confirmation measurements also improved personnel safety. The fewer the confirmation measurements that are taken, the less times the technicians need to open the line to manually obtain samples. This fits in line with Raylo’s strong commitment to implementing the highest precautions with all of its safety controls.

### **The chemistry is right**

“Overall, yields have increased and cycle times have been shortened. When you add the increase in quality, the improved pH readings by one sensor can be worth hundreds of thousands of dollars per year,” Pastushak says.



According to Pastushak, the 871 PH sensor is also very durable. “The one we deployed two years ago looks like it did the day we bought it. All we do is clean it after each use. The Ryton bodies are holding up extremely well. They display no degradation, pitting or corrosion even though we run the gamut of pH ranges, solvents, and aggressive conditions,” says Pastushak.

The Foxboro 871PH probe helps Raylo show its clients and the FDA just how much the company is dedicated to improving process control and product quality. “The sensor helps us prove that we can deliver on our production and quality promises,” says Pastushak.

During the past two years, Raylo has replaced three legacy probes within its manufacturing process and plans to replace three more. Raylo also has a second manufacturing facility with 15 probes that will eventually be swapped out as well.

But the benefits of Foxboro 871PH go far beyond improving Raylo’s bottom line. “By enabling us to increase product quality and yield, the Foxboro 871PH sensor has allowed us to do our job better so we can contribute to improving the quality of life for countless people and that’s what we’re in business for,” says Pastushak.